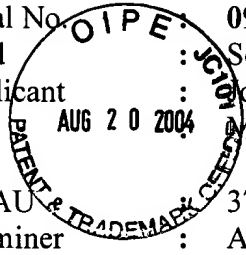


IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No. : 09/665,303
Filed : September 19, 2000
Applicant : John T. Santini, Jr., et al.
Title : Microchip Drug Delivery Devices
TC/AU : 3763
Examiner : A.T. Nguyen



Docket No. : 17648-0014
Customer No. : 29052

DECLARATION UNDER 37 C.F.R. § 1.132

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Robert S. Langer, hereby declare that:

1. I am an inventor of the above-identified patent application. I am the Kenneth J. Germeshausen Professor of Chemical and Biomedical Engineering at the Massachusetts Institute of Technology. A copy of my Curriculum Vitae is attached hereto.

2. I have over 500 issued or pending patents worldwide, many of which have been licensed or sublicensed to some 100 pharmaceutical, chemical, biotechnology, and medical device companies. I have over 30 years experience working in the fields of biotechnology and materials science, with an emphasis on drug delivery.

3. I have reviewed the Office Action mailed July 29, 2003, in connection with the present patent application. I also have reviewed U.S. Patent No. 6,114,658 to Roth et al. (hereinafter "the Roth patent") which is the English-language equivalent of the sole prior art

reference (WO 97/34697) relied upon by the Examiner for the rejections listed in the Office Action.

4. The Office Action mischaracterizes both the knowledge of one of ordinary skill in the art and the teachings of the Roth patent. The Office Action alleges “it is well-known to implant such a drug-carrying microsystem into a patient.” (page 2, second paragraph). This is incorrect. One of ordinary skill in the art at the time of our invention would not have considered implanting the microsystem of Roth into a patient. Prior to the publication of our priority applications, nothing in the prior art would have suggested an implantable microchip device packaged for implantation into a patient for the controlled release of drug molecules, wherein the device comprises multiple reservoirs containing drug molecules, releasable from the device by diffusion through or upon disintegration of reservoir caps.

5. The Office Action also mistakenly contends that “[p]harmaceuticals are, by their very nature, intended to be administered to the body, and thus *are only encapsulated in miniaturized devices for one reason, being placed in the body.*” (Page 7, third paragraph, emphasis added). On the contrary, a variety of storage and testing containment devices are never intended for implantation into a body.¹ A pharmaceutical compound can be “encapsulated” for a variety of reasons and in a variety of types and sizes of vessels over its useful life as it is

¹ In fact, the background of the Roth patent lists DE 3919042. The abstract of this patent describes

micromechanical structures with reservoirs used to test substances for possible changes in physical and/or chemical properties. ... The structure comprises a block and a cover.... The block has a number of depressions of particular size shape, distribution, etc., and the cover has elevations which match these exactly so as to provide a hermetic closure... These structures are used for evaluation and documentation in biotechnology, genetic engineering, cell or immune research, or for other medical ... research. They allow dangerous substances to be stored and handled (for testing, etc.) safely, and provide simple process control and evaluation of tests on very small amounts of sample.

manufactured, tested, packaged for bulk transport and storage, packaged in unit dosage forms, and finally readied for administration. Thus, pharmaceuticals are not encapsulated in microsystem devices only for placement in the body.

6. The Roth patent discloses that it is desirable to encapsulate sensitive materials, such as chemical indicator materials, catalysts, and pharmaceuticals (col. 1, lines 9-10), and that conventional methods for encapsulating such sensitive materials include “encapsulation of the substance in a glass bulb, plastic foils or similar packings” (col. 1, lines 20-22). One of ordinary skill in the art would have understood that a pharmaceutical could be encapsulated or packaged using devices and materials *unsuitable* for implantation. Accordingly, one of ordinary skill in the art would understand Roth as disclosing the encapsulation of a pharmaceutical into a miniaturized device only for the purpose of storage and *in vitro* testing of small samples of a potential pharmaceutical compound, such as in a drug discovery screening process.

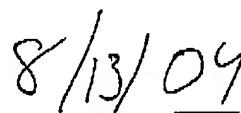
7. The Office Action also erroneously concluded that “whether Roth is merely testing the device or not, *one of ordinary skill would have found it obvious to implant the encapsulated drug device.*” (Page 7, third paragraph, emphasis added). This is not accurate. The Roth patent does not teach or suggest to one of ordinary skill in the art that they could implant into a patient the encapsulation devices disclosed in the Roth patent. The Roth patent also fails to provide any motivation to one of ordinary skill in the art to adapt or package the encapsulation devices for implantation and use *in vivo*.

8. The Roth patent failed to provide to one of ordinary skill at the time of the present invention any motivation to modify the devices disclosed in the Roth patent to achieve an implantable device for drug delivery as claimed in the present application. The rejections set

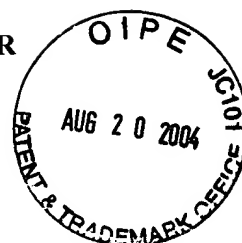
forth in the Office Action appear to be improperly based on hindsight reconstruction in view of the present application or other recent/non-prior art publications.

9. I declare that all statements made herein of my own knowledge and belief are true and that all statements made on information and belief are believed to be true, and further that the statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.


ROBERT S. LANGER


Date

ROBERT SAMUEL LANGER
Curriculum Vitae



DATE & PLACE OF BIRTH August 29, 1948, Albany, New York

EDUCATION

1974 Sc.D., Chemical Engineering, MIT

1970 B.S. (with distinction) Chemical Engineering, Cornell University

HONORS

- 2004 Charles F. Kettering Prize (GM Cancer Research Foundation)
- 2004 Pirkey Lectureship in Chemical Engineering (University of Texas, Austin)
- 2004 Evans Memorial Award Lectureship (Ohio State University)
- 2004 Nelson Taylor Lecturer and Awardee (Pennsylvania State University)
- 2004 Benjamin Zweifach Distinguished Lecturer (City College)
- 2004 Nelson Leonard Lecturer (University of Illinois)
- 2004 Donald Katz Lecturer (University of Michigan)
- 2003 Heinz Award for Technology, Economy and Employment
- 2003 Harvey Prize in Science and Technology and Human Health
- 2003 John Fritz Medal (American Association of Engineering Societies)
- 2003 Founders Lecturer (University of Wisconsin)
- 2003 Rohm and Hass Lecturer (Stanford University)
- 2003 Elected to the Academy of Achievement (Golden Plate Award)
- 2003 Tripathy Endowed Memorial Lecture (University of Massachusetts, Lowell)
- 2003 Skinner Memorial Lecture (Northwestern University)
- 2003 Honorary Doctorate (University of Liverpool, England)
- 2003 Maurice and Yetta Glicksman Lecturer (Brown University)
- 2003 FMC Lecturer (Princeton University)
- 2003 Seymour J. Kreshover Lecturer (National Institutes of Health)
- 2003 Whitaker Lecturer (American Society of Artificial Organs)
- 2002 Dickson Prize for Science (Carnegie Mellon University)
- 2002 Charles Stark Draper Award (National Academy of Engineering)
- 2002 Othmer Gold Medal (Chemical Heritage Foundation)
- 2002 Nagai Innovation Award (Controlled Release Society)
- 2002 Feigenbaum - Levine Lecturer (Beth Israel Hospital at Harvard Medical School)
- 2002 Honorary Doctorate (Hebrew University of Jerusalem)
- 2002 Herman Schwan Award (University of Pennsylvania)
- 2002 Distinguished Lecturer (University of Louisville)
- 2002 Institute Lecturer (American Institute of Chemical Engineers)
- 2001 Harrison Howe Award (American Chemical Society)
- 2001 Ulliyot Lecturer (Chemical Heritage Foundation)
- 2001 Clapp Lecturer (Brown University)
- 2001 Julian Smith Lecturer (Cornell University)
- 2001 Mason Lecturer (Stanford University)
- 2001 Distinguished Lecturer (Carnegie Mellon)
- 2000 Herman Beerman Lecturer (Society for Investigative Dermatology)
- 2000 Millennial Lecturer (University of Liverpool)
- 2000 Bayer Lecture (University of Pittsburgh)
- 2000 Bayer Stein Honorary Lecture (University of Massachusetts at Amherst)
- 2000 Honorary Doctorate (The Catholic University of Louvain, Belgium)
- 2000 Glaxo Wellcome International Achievement Award (Royal Pharmaceutical Society of Great Britain)
- 2000 Millennial Pharmaceutical Scientist Award (Millennial World Congress of Pharmaceutical Sciences)
- 2000 William G. Lowrie Lectureship (The Ohio State University)
- 2000 Frank T. Gucker Lecturer (Indiana University)
- 2000 First Pierre Galletti Award (American Institute of Medicine & Biological Engineering)
- 2000 First Patten Distinguished Lectureship (University of Colorado at Boulder)

2000 Wallace Carothers Award (American Chemical Society, Delaware Section)
 1999 American Chemical Society Award in Polymer Chemistry
 1999 Esselen Award (American Chemical Society, Northeast Section)
 1999 G.N. Lewis Medal and Lecturer (University of California at Berkeley)
 1999 Beckman Lecturer (University of Illinois at Urbana)
 1999 Reilly Lecturership (Notre Dame University)
 1999 Ebert Prize (American Pharmaceutical Association)
 1998 Outstanding Pharmaceutical Paper Award (Controlled Release Society)
 1998 Lemelson-MIT Prize for Invention and Innovation
 1998 The Nagai Foundation Tokyo International Prize
 1998 Wagner Lectureship (University of Michigan)
 1998 Ewing Halsell Foundation Lectureship (University of Texas Health Center, San Antonio)
 1998 Robert R. Linton Distinguished Lecture; New England Society for Vascular Surgery
 1998 Marcus Memorial Lecturer (Washington University, St. Louis)
 1998 Joseph Stokes, Jr. Lecturnship (University of Pennsylvania)
 1997 Killian Faculty Achievement Award (MIT)
 1997 Wiley Medal (U.S. Food and Drug Administration)
 1997 Honorary Doctorate (The Technion - Israel)
 1997 William J. Rashkind Memorial Lecture (American Heart Association)
 1997 Rohm and Haas Lecturer in Materials Chemistry (University of North Carolina)
 1996 Gairdner Foundation International Award
 1996 Honorary Doctorate (Eidgenossische Technische Hochschule-ETH, Switzerland)
 1996 William Walker Award (American Institute of Chemical Engineers)
 1996 Society of Plastics Engineers International Award
 1996 Ebert Prize (American Pharmaceutical Association)
 1996 Elected a Fellow of Biomaterials Science and Engineering
 1996 The Berkeley Lecturer (University of California, Berkeley)
 1996 Avis Distinguished Visiting Professor (University of Tennessee)
 1995 International John W. Hyatt Service to Mankind Award (Society of Plastics Engineers)
 1995 Ebert Prize (American Pharmaceutical Association)
 1995 Distinguished Medical Scientist Lecturer (Ohio State University)
 1995 Lacy Lecturer (California Institute of Technology)
 1995 Ralph Peck Memorial Lecturer (Illinois Institute of Technology)
 1995 Elected a Fellow (American Association of Pharmaceutical Scientists)
 1995 PEL Associates Award (PEL Associates, Groton, Connecticut)
 1994 Whitaker Distinguished Lecturer (Biomedical Engineering Society)
 1994 Elected to the American Academy of Arts and Sciences
 1994 Elected a Fellow, Society of Biomaterials
 1994 Miles Lecturer (Cornell University)
 1994 Feigenbaum Memorial Lecturer (Beth Israel Hospital, Harvard Medical School)
 1993 Distinguished Pharmac. Scientist Award (Highest Honor of the Amer. Assoc.of Pharm.Scient.)
 1993 Kurt Wohl Memorial Lecturer (University of Delaware)
 1993 Priestley Lecturer (Penn State University)
 1992 Elected to the National Academy of Sciences
 1992 Elected to the National Academy of Engineering
 1992 American Chemical Society Award for Applied Polymer Science (Phillips Award)
 1992 Perlman Memorial Award Lecturer (American Chemical Society, Biochemical Technology Division)
 1992 Elected a Founding Fellow, American Institute of Medical and Biological Engineering
 1992 Kelly Distinguished Lecturer (Purdue University)
 1992 Miles Distinguished Lecturer (University of Pittsburgh)
 1992 Outstanding Pharmaceutical Paper Award (Controlled Release Society)
 1991 Organon Teknika Award (European Society for Artificial Organs)
 1991 Charles M.A. Stine Award in Materials Science and Eng. (Am. Institute of Chem.Eng.)
 1991 Louis W. Busse Lecturer (University of Wisconsin)

1991 Sidney Riegelman Lecturer (University of California, San Francisco)
 1991 Ashton-Cary Lecturer (Georgia Institute of Technology)
 1991 Sandoz-Dorsey Lecturer (Ohio State University)
 1990 Professional Progress Award (American Institute of Chemical Engineers)
 1990 Clemson Award for Basic Research (Society for Biomaterials)
 1990 Outstanding Pharmaceutical Paper Award (Controlled Release Society)
 1989 Elected to the Institute of Medicine of the National Academy of Sciences
 1989 Creative Polymer Chemistry Award (American Chemical Society, Polymer Division)
 1989 Outstanding patent in Massachusetts and one of the twenty outstanding patents in the U.S. (Intellectual Property Owners, Inc.)
 1989 Founders Award for Outstanding Research (Controlled Release Society)
 1989 Walter F. Enz Lecturer (University of Kansas)
 1988 Elected to the Gordon Conference Research Council
 1988 Elected Chairman, Gordon Conference on Drug Carriers in Biology and Medicine
 1988 Robert Rushmer Lecturer (University of Washington, Seattle)
 1988 1st Presidential Lecturer, Controlled Release Society (Basel, Switzerland)
 1987 Biomedical Research Council Lecturer (University of Michigan)
 1986 Food, Pharmaceutical and Bioengineering Award (American Institute of Chemical Engineers)
 1986 Elmer L. Linseth Lecturer (Case Western Reserve University)
 1983 Outstanding Paper, Institute of Electrical and Electronic Engineering
 1983 Merck, Sharpe and Dohme Lecturer (University of Puerto Rico)
 1982 Paper Listed as One of the Outstanding Papers of the Year, CHEMTECH
 1982 Recipient of the first Dorothy W. Poitras Chair, MIT
 1982 Outstanding Teacher Award, MIT Graduate Student Council

EMPLOYMENT

7/88- Kenneth J. Germeshausen Professor of Chemical and Biomedical Engineering, MIT Department of Chemical Engineering; Whitaker College of Health Sciences, Technology, and Management; and the Harvard-MIT Division of Health Sciences and Technology
 7/99-6/00 Senior Lecturer on Surgery, Harvard University, Harvard Medical School
 7/85-6/88 Professor of Biochemical Engineering, MIT, Department of Applied Biological Sciences, Whitaker College of Health Sciences, Technology, and Management, and the Harvard-MIT Division of Health Sciences and Technology
 7/81-6/85 Associate Professor of Biochemical Engineering, MIT, Department of Nutrition and Food Sciences and the Whitaker College of Health Sciences Technology, and Management, and the Harvard-MIT Division of Health Sciences and Technology
 7/78-6/81 Assistant Professor of Nutritional Biochemistry, MIT, Department of Nutrition and Food Sciences
 7/77-6/78 Assistant Professor of Nutritional Biochemistry, MIT (Visiting), Department of Nutrition & Food Sciences
 7/74-present Research Associate, Children's Hospital Medical Center, Harvard Med. School, Boston, MA
 9/72-6/74 Research Assistant, MIT
 9/72-8/73 Chairman, Math and Science Departments, The Group School, Cambridge, MA

PROFESSIONAL AND ACADEMIC ORGANIZATIONS

Controlled Release Society (Elected President, 1991-1992) (Elected to Board of Governors, 1981-1985; Chairman, Regulatory Affairs Committee, 1985-1989).
 Biomedical Engineering Society (Elected to the Board of Directors, 1991-1994)
 American Institute of Chemical Engineers (Food, Pharmaceutical and Bioeng. Division)
 American Chemical Society (Polymer Division)
 American Society of Artificial Internal Organs (Program Committee 1984-1987; Membership Committee (1991-93)
 International Society of Artificial Internal Organs
 Scientific Advisory Board, Department of Chemical Engineering, Georgia Institute of Technology (1992-2000)
 Society for Biomaterials (Elected a Fellow, 1994)
 American Association of Pharmaceutical Scientists (Elected a Fellow, 1995)

American Institute of Medical and Biological Engineers (Elected Founding Fellow, 1992; Elected Chair, College of Fellows, 1995)

The Science Board, the United States Food and Drug Administration (FDA) (highest Advisory Board of the FDA), 1995--2002 (Chair from 1999 -- 2002)

Scientific Advisory Board, Schepens Eye Institute, Harvard Medical School (1995-1998)

Board of Scientific Counselors, National Institutes of Health Center for Research Resources (1996-2001)

Scientific Advisory Board, Division of Chemistry and Chemical Engineering, California Institute of Technology (1999-)

Scientific Advisory Board, Department of Chemical Engineering, Princeton University (1999-)

Board of Overseers, Othmer Research Institute, Brooklyn Polytechnic Institute (2001-)

Board of Directors, McGovern Institute, Massachusetts Institute of Technology (2001-)

Board of Directors, Whitehead Institute (2003)

Chair, Killian Award Committee (2004)

COURSES TAUGHT

20.002U	(1977 - 1988)	Laboratory in Applied Biology
20.S35	(1979 - 1988)	Pharmacological Engineering
20.11G	(1979 - 1988)	Analytical Practices in Biochemistry
HST 110	(1979 - 1981)	Renal Pathophysiology
20.113	(1987 - 1988)	Problems in Biotechnology
10.02J	(1989 -)	Biotechnology and Engineering
10.361	(1989 -)	Integrated Chemical Engineering
10.13	(1989 -1991)	Thermodynamics
10.984	(1990 -)	Biomedical Applications of Chemical Engineering
10.26	(1992 -)	Senior Chemical Engineering Project Laboratory

MIT ACTIVITIES

1972-73, 80-	Board of Trustees, MIT Community Service Fund
1972-74	Committee on Preprofessional Advising and Education, MIT
1972-74	Steering Committee, Urban Action, MIT
1977-85	Freshman Advisor
1978-	Undergraduate Advisor
1980-	Premedical Advisory Council, MIT
1977-80	Seminar Committee, Department of Applied Biological Sciences, MIT
1978-80	Asinari Committee, MIT
1979-88	Undergraduate Affairs Committee, Department of Applied Biological Sciences, MIT (Chairman, 1981-1985)
1980-84	MIT-Wellesley Upward Bound Joint Steering Committee
1981-82, 84-85	Financial Aid Committee, Department of Applied Biological Sciences, MIT
1981-86	Admissions Committee, Harvard-MIT Division of Health Sciences and Technology
1983-87	Curriculum Committee, Dept. of Applied Biological Sciences (Chairman, 1985-1987)
1983-87	Radiation Committee, MIT
1983-97	Sea Grant Committee, MIT (Chairman, 1993-1997)
1985-87	Admissions Committee, Harvard MD-POD Program
1986-92	Admissions Committee, MIT Medical Engineering-Medical Physics Program
1986-	Harvard-MIT Joint Committee on Health Sciences and Technology
1988	Search Committee for Department Head, Department of Chemical Engineering
1988-1992	Admissions Committee, Department of Chemical Engineering
1989-1991	Undergraduate Committee, Department of Chemical Engineering
1991-1993	Seminar Chairman, Department of Chemical Engineering
1993-	Board of Advisors, MIT Industrial Summer Session Program
1994-1995	Selection Committee for Co-Director of Harvard-MIT HST Program
2000-	Harvard-MIT Division of Health Sciences and Technology Advisory Council

EDITORIAL BOARDS

1983-2002	BIOMATERIALS- Editor
1987-	BIOMATERIALS, ARTIFICIAL CELLS, AND IMMOBILIZATION TECHNOLOGY (Associate Editor, 1991-)
1983-92	SELECTIVE CANCER THERAPEUTICS (CANCER DRUG DELIVERY)
1983	METHODS OF ENZYMOLOGY-DRUG DELIVERY SYSTEMS
1984-98	JOURNAL OF CONTROLLED RELEASE
1985-	BIOMEDICAL POLYMERS
1986-	ADVANCED DRUG DELIVERY SYSTEMS
1987-	DRUG DESIGN AND DELIVERY
1990-	MARINE BIOTECHNOLOGY
1991-94	CHEMISTRY OF MATERIALS
1991 -	CELL TRANSPLANTATION
1991 -	POLYMERS FOR ADVANCED TECHNOLOGIES
1991 -	DRUG TARGETING AND DELIVERY
1992-	INTERNATIONAL JOURNAL OF DRUG TARGETING
1992-	JOURNAL OF BIOACTIVE AND COMPATIBLE POLYMERS
1994-98	CANCER BIOTHERAPY AND RADIOPHARMACEUTICALS
1994-	JOURNAL OF PHARMACEUTICAL SCIENCE
1995-	TISSUE ENGINEERING
1995-	THE ENCYCLOPEDIA OF CONTROLLED DRUG DELIVERY
1996-	BIRKHAUSER: SYNTHETIC BIODEGRADABLE POLYMER SCAFFOLDS
1996-98	CHEMICAL AND ENGINEERING NEWS
1997-99	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES
1997-	ANNUAL REVIEWS OF BIOMEDICAL ENGINEERING
1997-	BIOMEDICAL MICRODEVICES
1998-	DIABETES TECHNOLOGY & THERAPEUTICS
1999-	JOURNAL OF POLYMER SCIENCE, CHEMISTRY
1999-	PHARMACEUTICAL SCIENCE
1999-	REGENERATIVE MEDICINE
1999-	METHODS OF TISSUE ENGINEERING
1999-	ANGEWANDTE CHEMIE
2000-	EUROPEAN JOURNAL OF PHARMACEUTICAL SCIENCES
2002-	JOURNAL OF INVESTIGATIVE DERMATOLOGY-Associate Editor
2004-	MECHANICS AND CHEMISTRY OF BIOSYSTEMS

PUBLICATIONS

1. Gardner, C., Colton, C., Langer, R., Hamilton, B., Archer, M. and Whitesides, G., Enzymatic regeneration of ATP from AMP and ADP I. thermodynamics, kinetics, and process development, in Enzyme Engin., 1974, 2: 209-216, Pye, E. and Wingard, L. eds., Plenum Press, New York.
2. Gardner, C., Langer, R. and Colton, C., Dependence of pH of the hydroxylamine assay for acyl phosphates. Analy. Biochem., 76: 654-656, 1976.
3. Kessler, D., Langer, R., Pless, N. and Folkman, J., Mast cells and tumor angiogenesis. Int. J. Cancer, 18: 703-709, 1976.
4. Langer, R., Hamilton, B., Gardner, C. Archer, M. and Colton, C., Enzymatic regeneration of ATP I alternative routes. AIChE J., 22: 1079-1090, 1976.
5. Langer, R., Brem, H., Falterman, K., Klein, M. and Folkman, J., Isolation of a cartilage factor that inhibits tumor neovascularization. Science, 193: 70-72, 1976.
6. Langer, R. and Folkman, J., Polymers for the sustained release of proteins and other macromolecules. Nature, 263: 797-800, 1976.
7. Brem, S., Preis, I., Langer, R., Brem, H., Folkman, J. and Patz, A., Inhibition of neovascularization by an extract derived from vitreous. Am. J. Ophthal., 84: 323-328, 1977.
8. Klagsbrun, M., Langer, R., Levenson, R., Smith, S. and Lillehei, C., The stimulation of DNA synthesis and cell division in chondrocytes and 3T3 cells by a growth factor isolated from cartilage. Exp. Cell Res., 105: 99-108, 1977.
9. Langer, R., Gardner, C. and Colton, C., Enzymatic regeneration of ATP II: Equilibrium studies with acetate kinase and adenylate kinase. AIChE J., 23: 1-10, 1977.
10. Nemet, M., Solomon, B., Langer, R. and Colton, C., Enzymatic regeneration of ATP from AMP and ADP: III kinetic studies with the coupled enzyme system, in Enzyme Eng., 1977, 3: 85-91, E. Pye, ed., Plenum Press, New York.
11. Conn, H. and Langer, R., Continuous long-term intra-arterial infusion in the unrestrained rabbit. Lab. Anim. Sci., 28: 598-602, 1978.
12. Langer, R. and Folkman, J., Sustained release of macromolecules from polymers, in Poly. Del. Systems, Midland Macro. Monograph, 1978, 5: 175-196, R. Kostelnik, ed., Gordon and Breach, New York.
13. Augustin, A. and Langer, R., Inhibitors to tumor vascularization and their delivery systems: possible extension to diabetes research, in Ocular and Systemic Disorders, 1979, 33-36, R. Fair, ed., American Optometric Association, St. Louis.
14. Tapper, D., Langer, R., Conn, H. and Folkman, J., Oxygen content determined by acrylamide polymerization: screening of anticancer agents, generation of oxyhemoglobin dissociation curves and potential applications. Ann. Surg., 189: 275-283, 1979.
15. Preis, I. and Langer, R., A single-step immunization by sustained antigen release. J. of Immuno. Meth., 28: 193-197, 1979.
16. Tapper, D., Langer, R., Bellows, A. and Folkman, J., Angiogenesis capacity as a diagnostic marker for human eye tumors. Surgery, 86: 36-40, 1979.
17. Rhine, W., Hsieh, D. and Langer, R., Polymers for sustained macromolecule release: Procedures to fabricate reproducible delivery systems and control release kinetics. J. Pharma. Sci., 69: 265-270, 1980.
18. Conn, H., Berman, M., Kenyon, K., Langer, R. and Gage, J., Stromal vascularization prevents corneal ulceration. Invest. Ophthal., 19: 362-370, 1980.
19. Creque, H., Langer, R. and Folkman, J., One month sustained release of insulin from a polymer implant. Diabetes 29: 37-41, 1980.
20. Augustin, A. and Langer, R., Studies of inhibitors to tumor neovascularization and their delivery systems, Diabetes, 29: 33-35, 1980.
21. Langer, R., Fefferman, M., Gryska, P. and Berman, K., A simple method for studying chemotaxis using sustained release of attractants from inert polymers. Can. J. Microbiol., 26: 274-278, 1980.
22. Langer, R., Conn, H., Vacanti, J., Haudenschild, C. and Folkman, J., Control of tumor growth in animals by infusion of an angiogenesis inhibitor. Proc. of the Nat. Acad. of Sci., 77: 4331-4335, 1980.
23. Langer, R., Polymeric delivery systems for controlled drug release. Chem. Eng. Commun., 6: 1-48, 1980.

24. Langer, R. and Folkman, J., Controlled release of macromolecules from polymers, in Biomedical Poly., 1980, 113-139, E. Goldberg, A. Nakajima eds., Academic Press, New York.
25. Langer, R., Rhine, W., Hsieh, D. and Bawa, R., Polymers for the sustained release of macromolecules: Applications and control of release kinetics, in Contr. Rel. of Bioactive Mat., 1980, 83-98, R. Baker, ed., Academic Press, New York.
26. Langer, R., Rhine, W., Hsieh, D. and Folkman, J., Control of release kinetics of macromolecules from polymers., J. Memb. Sci., 7: 333-350, 1980.
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28. Folkman, J., Ausprunk, D. and Langer, R., Connective tissue: Small blood vessels and capillaries, in Textbook of Rheumatology, 1981, 210-220, W. Kelly, E. Harris, S. Ruddy, C. Sledge, eds., W.B. Saunders Co.
29. Conn, H., Langer, R., Iodine disinfection of hydrophilic contact lenses, Ann. Ophthal., 13: 361-364, 1981.
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31. Hsieh, D., Langer, R., Folkman, J., Magnetic modulation of release of macromolecules from Polymers. PNAS 78: 1863-1867, 1981.
32. Galliher, P., Cooney, C., Langer, R., Linhardt, R., Heparinase production by flavobacteria, Appl. Env. Microbiology, 41: 360-365, 1981.
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34. Langer, R., Controlled Release: A new approach to drug delivery, Tech. Rev., 83: 26-34, 1981.
35. Langer, R., Karel, M. Controlled release technology: Polymers in medicine, food and agriculture. Poly. News, 7: 250-258, 1981.
36. Langer, R., Hsieh, D., Brown, L., Rhine, W., Polymers for the sustained release of macromolecules: Controlled and magnetically modulated systems, in Better Therapy With Existing Drugs: New Uses and Del. Sys., 1981, 179-216, A. Bearn ed., Merck & Co., Biomedical Information Corporation, New York.
37. Hsieh, D., Langer, R., Experimental approaches for achieving both zero-order and modulated controlled release from polymer matrix systems, in Cont. Rel. of Pesticides and Pharm., 1981, 5-16, D. Lewis ed., Plenum Press, NY.
38. Langer, R., Folkman, J., Angiogenesis Inhibitors in molecular actions and targets for cancer chemotherapeutic agents, 1981, 511-525, A. Sartorelli, J. Lazo, J. Bertino, eds., Academic Press, New York.
39. Langer, R., Hsieh, D., Peil, A., Bawa, R., Rhine, W., Polymers for controlled release of macromolecules: Kinetics, applications, external control, in Cont. and Topical Rel. of Drugs to the Body, 1981, 206: 10-20, S. Chandrasekaran, J. Eckenhoff, eds., AIChE Symposium Series.
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41. Moskowitz, M., Mayberg, M., Langer, R., Controlled release of horseradish peroxidase from polymers: A method to improve histochemical localization and sensitivity, Brain Res., 212: 460-465, 1981.
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43. Langer, R., Urquhart, J. Blackshear, P., Implantable drug delivery systems, Trans. Am. Soc. Art. Int. Organs, 27: 648-654, 1981.
44. Peil, A., Barrett, F., Rha, C., Langer, R., Retention of micro-nutrients by polymer coatings used to fortify rice, J. Food Science, 47: 260-262, 1981.
45. Langer, R., Linhardt, R., Klein, M., Flanagan, M., Galliher, P., Cooney, C., A system for heparin removal, in Biomaterials: Interfacial Phenomena and Applications, 1982, 493-509, S. Cooper, A. Hoffman, N. Peppas, B. Rattner, eds., Advances in Chemistry Series, Washington, DC.
46. Berman, M., Winthrop, S., Ausprunk, D., Rose, J., Langer, R., Gage, J., Plasminogen activator (urokinase) causes vascularization of the cornea. Invest. Ophthal., 22: 191-199, 1982.
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